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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/771,257	02/03/2004	Antonino Cattaneo	18396/2272	2419

29933 7590 04/14/2008
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EXAMINER	
SIMS, JASON M	

ART UNIT	PAPER NUMBER
1631	

MAIL DATE	DELIVERY MODE
04/14/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/771,257	CATTANEO ET AL.	
	Examiner	Art Unit	
	JASON M. SIMS	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 January 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *1-13 and 15-19* is/are withdrawn from consideration.

5)☒ Claim(s) *20* is/are allowed.

6)☒ Claim(s) *14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1/9/2008 has been entered.

Claims 1-13 and 15-19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventive group, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 9/18/2006.

Applicant has newly added claim 20 in the response filed 1/9/2008, which has been entered.

Claims 14 and 20 are the current claims hereby under examination.

Claim Rejections - 35 USC § 103

Response to Arguments:

Applicant's arguments, filed 1/9/2008, with respect to the rejection of claims under 35 USC 103 have been fully considered and are persuasive because of applicant's amendment and arguments. Therefore the rejection has been withdrawn.

The following rejection has been newly added and has been necessitated by amendment:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 14 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). These factors include, but are not limited to:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;
(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of the claims

The claim is broad because the claim encompasses an intracellularly binding immunoglobulin molecule comprising a variable heavy chain which exhibits at least 95% homology to the consensus sequence SEQ ID No 3; and a variable light chain.

Therefore, the claim encompasses a 5% variability within the variably heavy chain to the consensus sequence SEQ ID No 3, which comprises 112 amino acid residues and 5% equals approximately 5.6 amino acid residues. Essentially, there may be a 5.6 residue difference from SEQ ID No. 3, such as the first 5-6 amino acids, with each residue having 4 options, which results in approximately 983 unique combinations at one time. The number of unique combinations increases dramatically again when taking into consideration the number of combinations involving the 5-6 residues that may vary throughout the entire SEQ ID No. 3.

The nature of the invention

The invention is drawn to an intracellularly binding immunoglobulin molecule comprising a variable heavy chain which exhibits at least 95% homology to the consensus sequence SEQ ID No 3.

The state of the prior art and the level of predictability

A number of scientific challenges are present in understanding a correlation between varying amino acid residues in a variable heavy chain while maintaining binding function or will maintain its intracellular binding. Generally, there are number of art-related disclosures that illustrate that the art as it pertains to the claimed invention is unpredictable. It is understood from the instant specification that SEQ ID No. 3 is a conserved sequence in the variable heavy chain. A conserved sequence within a binding domain typically involves key residues for maintaining function. Therefore, a substitution of one amino acid or even 5-6 amino acid substitutions of key residues can have unpredictable results. For example, Chiba et al. (P/N 5,171,838) at col. 5, lines 3-5 describes that “a particular amino acid substitution on Leu3a binding activity is often

somewhat unpredictable." Chiba et al. does teach that certain "key" residues may be readily substituted without sacrifice of biological activity, but these are known residues in the instant reference. Boehncke et al. (1992) in the abstract teaches that particular amino acid substitutions such as those substitutions with larger side chains often diminished activity. Furthermore, Boehncke et al. (1992) teaches at the abstract that the change in the peptide altered the extent of binding. In addition, Lowman et al. (US A/N 2003/0228663) at paragraph [0256] states that "these types of substitutions in general had unpredictable effects on binding affinity."

The amount of guidance and existence of working examples

In the detailed description of the specification and in Fig. 5 applicants describe an intracellularly binding immunoglobulin comprising a variable heavy chain, which exhibits a variety of homology to the consensus sequence SEQ ID No 3. However, there were no examples found that described which amino acid residues could be substituted without unpredictably effecting the binding function of the immunoglobulin. Therefore, there is not found guidance as to which 5% of the amino acid substitutions of consensus sequence SEQ ID No 3 would cause the immunoglobulin to maintain binding functionality.

The Quantity of Experimentation

Based on the art cited above, the unresolved issues in the relevant art pertaining to the unpredictability of protein function based on amino acid substitutions, the amount of non-routine experimentation required would be high. It is well known in the art that single or multiple substitutions or deletions can alter biomolecular function in many

instances, albeit not all. In the absence of any factual evidence that characterizes the structural and functional components of a biomolecule, the effects of these changes are largely unpredictable as stated above. In the instant specification it is unclear as to which residues are “key” residues in Seq ID No 3 and therefore it is unpredictable as to which amino acid substitutions will enable the immunoglobulin to maintain its binding function. Without such information as to the "key" binding residues of the variable heavy chain, the amount of experimentation necessary to determine which amino acid substitutions would not result in a lack of binding functionality would be undue.

Accordingly, in order to enable the invention as claimed, one of ordinary skill in the art would have to resort to undue experimentation.

Allowable Subject Matter

Claim 20 is allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jason Sims, whose telephone number is (571)-272-7540.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner’s supervisor, Marjorie Moran can be reached via telephone (571)-272-0720.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the Central PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The Central PTO Fax Center number is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for

published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

// Jason Sims //
/Michael Borin, Ph.D./
Primary Examiner, Art Unit 1631